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Synthesis of novel glycopeptidomimetics via N$^{\beta}$-protected-amino alkyl isonitrile based Ugi 4C reaction

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ABSTRACT

The Ugi-4C reaction employing N$^{\beta}$-protected-amino alkyl isonitrile, amino acid ester, aldehyde, and glycosyl acid has resulted in novel glycosylated peptidomimetics. The extension of MCR products for the synthesis of *N*,*N*′-orthogonally protected glycosylated peptidomimetics has also been demonstrated.

Isonitriles have unique reactive features due to their ability to form reactive α-adducts on reaction with both nucleophiles and electrophiles at the same atom under mild conditions. Isonitrile based multicomponent reactions[1,2] (IMCRs) such as Ugi four-component reaction[3] (U4CR) and Passerini three-component reaction[4] (P3CR) have shown tremendous synthetic potential for the convergent synthesis of plethora of diverse molecular scaffolds over the last decade. The U4CR involves mainly, condensation of an amine, aldehyde, isonitrile, and a carboxylic acid bearing substrates to generate a plethora of peptide-like molecules.[5–7] Robustness of this reaction makes it possible to access molecular complexity and diversity which is useful for organic synthesis and drug discovery program, simply by suitable design of the starting materials in an atom- and step-economical way. Thus far, the majority of the reports on Ugi-MCR have employed isocyano esters/carboxamides that are prepared by the dehydration of formyl-amino esters/amides as the isonitrile components.[4b] N$^{\beta}$-protected amino alkyl isonitriles prepared through carboxy modification of corresponding β-amino acids were first reported by our group as an alternate class of isonitriles derived from amino acids.[8] Switching the isonitrile position from N- to C-terminus of the amino acid skeleton leads to an entirely new repertoire of Ugi products that were hitherto not accessible by classical isonitrile esters. Presently, we are engaged in demonstrating its synthetic utility in isonitrile based MCRs leading to novel peptidomimetics as well as glycopeptidomimetics.[9]

Glycopeptides play a significant role in cell growth regulation, cancer cell metastasis, protein folding, cell adhesion, viral, bacterial, and parasitical infections.[10,11] Also there is a pressing need for methods that provide access to glycopeptides to explore various biological functions such as in cellular differentiation, cell–cell communication, immune response, and also for the development of glycopeptide-based drugs with improved pharmacokinetic properties.[12] Due to this wide spread application several groups have reported the synthesis of glycopeptide derivatives via Ugi four-component condensation (4CC) reaction.[13–15] Recently, Volonterio and co-workers reported the synthesis of diverse peptide sugar conjugates through a regiospecific four-component reaction.[16] Thus in view of their biological significance there is an untiring interest over the protocols that generate diverse glycopeptides and glycopeptidomimetics.[17] An interesting application of N-protected-β-amino alkyl isonitriles in the Ugi MCR for generating a new variety of glycosylated peptidomimetics has been demonstrated in the present work.

To execute the designed protocol, the essential starting materials are N-protected-β-amino alkyl isonitriles, sugars equipped with a carboxylic group, α-amino alkyl esters, and commercially available aldehydes. N$^{\beta}$-protected amino alkyl isonitriles were prepared as reported by us previously.[8] A further task at this stage was to equip sugar components with a carboxy group, that is, to install a carboxy group on the sugar or to attach a carboxy functionalized molecule to a suitably protected sugar. Thus, three different kinds of sugar acids were prepared following established protocols[18–23] and employed in this study (Fig. 1).

For the synthesis of galactose-6-acid **1**, initially, α-D-galactose was protected as (1,2),(3,4)-diacetylgalactopyranose by treating

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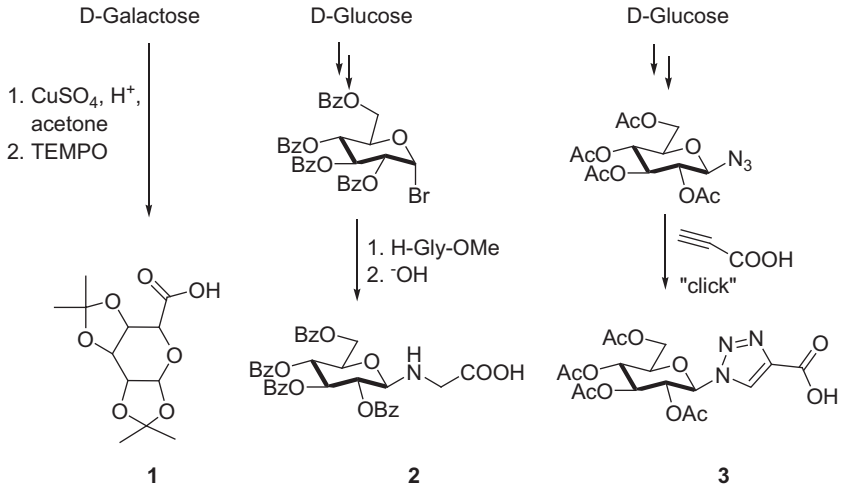


Figure 1. Sugar acids employed in Ugi-MCR.

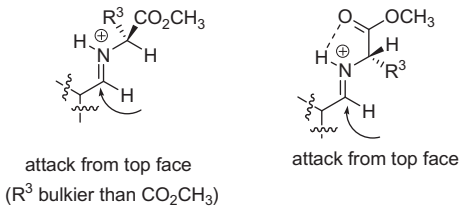
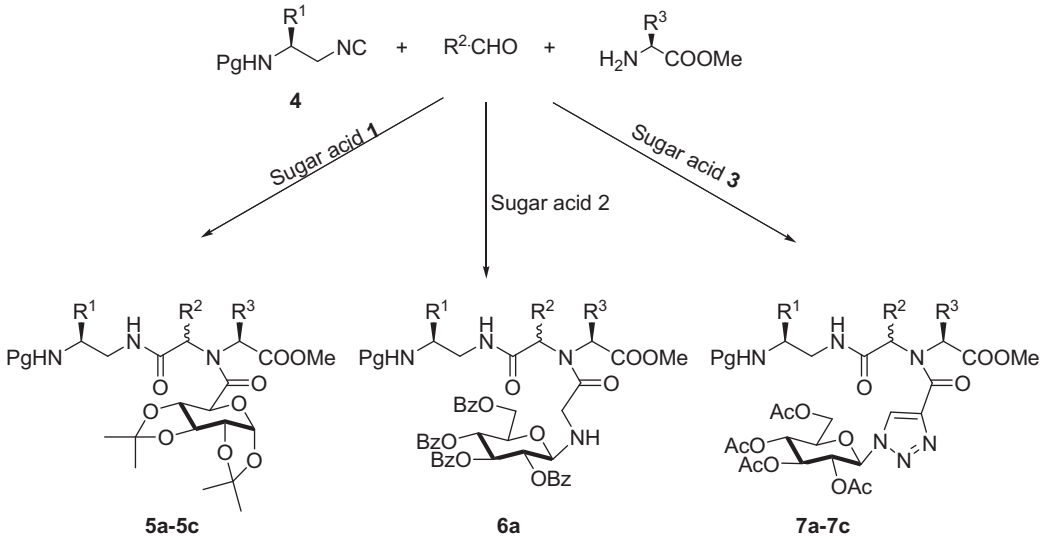


Figure 2. Conformations of protonated iminium ion of amino acid ester for high diastereoselectivity via Ugi-MCR.

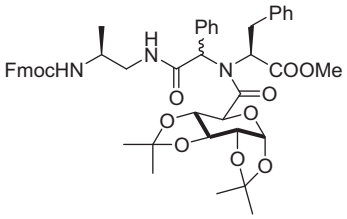
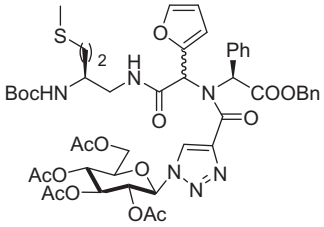
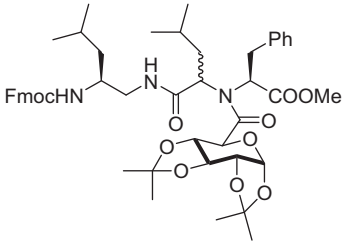
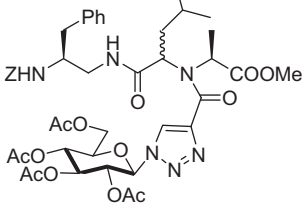
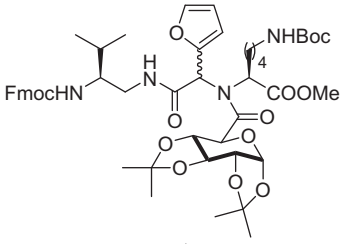
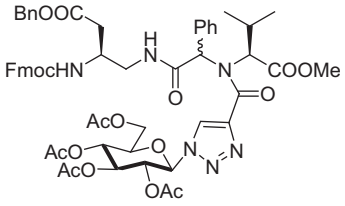
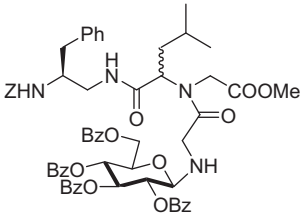
with $CuSO_4$/cat. H_2SO_4 in acetone and later subjected to oxidation using (2,2,6,6-tetramethylpiperidin-1-yl)oxyl [TEMPO] to convert C_6–CH_2OH into COOH.[18] The glycosyl acid **2** was obtained by a reaction of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl-1-bromide[19] with Gly-OMe in the presence of K_2CO_3 followed by the ester hydrolysis. The sugar acid **3** was prepared by Cu-mediated 'click' reaction of sugar-1-azide with propiolic acid.[20,21] The latter molecule would be interesting by itself owing to the presence of biologically significant triazole moiety.[20,22,23] Commercially available benzaldehyde, isovaleraldehyde, and furfuraldehyde were used as the aldehyde components, while methyl esters of several amino acids as amine components in the present work.

In an initial experiment, equimolar quantities of benzaldehyde and H-Phe-OMe were stirred in MeOH to generate an imine. After the complete formation of the imine (by TLC analysis), Fmoc-Ala-ψ[CH_2NC] **4a** and (1,2),(3,4)-diacetylgalactopyranosyl-6-acid **1** in MeOH were added. The reaction mixture was stirred at rt for 48 h. A simple aqueous work-up followed by chromatographic purification afforded the glycoconjugate **5a** in 85% yield.[24] However, the possible diastereomers generated due to the new chiral center at aldehydic carbon, could not be separated through column chromatography. The chiral HPLC analysis of **5a** showed the diastereomers in 97.5:2.5 ratio.[25] The high diastereoselectivity observed for the Ugi 4CR product can be attributed to the use of amino acid ester as the amine component, which is in agreement with the earlier reports.[3,9,26] According to the well known Ugi-4CC mechanism, diastereoselectivity can be explained by the preferential attack of carbenoid carbon of isocyanide on protonated imine from top face, as described in Figure 2. In a similar way, two other glycosylated



Scheme 1. Synthesis of N-glycosylated peptidomimetics via Ugi-MCR.

Table 1
List of Ugi products prepared

Entry	Ugi construct	Yield (%)	HRMS [M+Na]$^+$ obsd (calcd)	Entry	Ugi construct	Yield (%)	HRMS [M+Na]$^+$ obsd (calcd)
5a		85	870.3571 (870.3578)	**7a**		76	1029.40[a] (1029.35)
5b		83	892.4361 (892.4360)	**7b**		82	931.3701 (931.3701)
5c		80	969.45 (969.45)[a]	**7c**		78	1125.40 (1125.41)[a]
6a		81	1127.4269 (1127.4266)				

[a] ESI-MS.

peptides **5b** and **5c** were obtained based on sugar acid **1**. In the next set of experiments sugar acid components **2** and **3** were also used successfully in the Ugi MCR to afford corresponding adducts **6a** and **7a–c** (Scheme 1, Table 1) [27]. Chiral HPLC analysis of the products **6a** and **7a** revealed two peaks corresponding to the two diastereomeric products in the ratios 97:3 and 95:5, respectively.

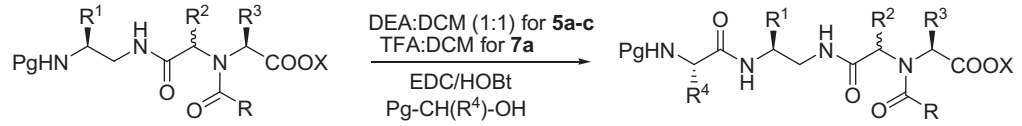
Thus obtained Ugi-adducts were stable and available to be inserted into a peptide chain upon deprotection of either terminus as per the design. We demonstrated terminal extensions on a few selected Ugi-adducts either by N-deprotection and coupling with another N-protected amino acid or by hydrolysis of the ester followed by carboxy activation and coupling to an amine head (Scheme 2).

In the second part of the study, another variety of glycopeptidomimetics viz., *N*,*N*′-orthogonally protected glycosylated peptides were prepared simply by exchanging the amine and carboxy contributors in the above described reaction. In effect, the reaction involved 2,3,4,6-tetra-*O*-acetyl-glucopyranosyl-1-amine and an N^{α}-protected amino acid along with N^{β}-protected amino alkyl isonitrile and aldehyde. Orthogonality for the N-protecting groups of the participating reactants viz., isonitrile and acid was maintained so as to enable selective deprotection/chain extension after the assembly of MCR adducts (Scheme 3). Thus **12a** and **12b** were obtained in 88% and 85% yields, respectively, using a combination of Fmoc/Z and Z/Boc groups, respectively. The reaction was facile and the products were characterized by NMR and mass spectral analyses. The orthogonality of the protecting groups on compounds **12** allowed the selective chain extension on either terminus which was demonstrated by preparing **13a** and **13b** from their parent Ugi-adducts **12a** and **12b**, respectively (Scheme 4).

In summary, N-protected amino alkyl isonitriles have been employed in the Ugi multi-component reaction for constructing a new class of neoglycopeptidomimetics. Three different types of glycosyl acids were employed to obtain novel Ugi scaffolds. All the Ugi-adducts are isolated as stable compounds, characterized, and some of them were engaged in chain extension on either terminus to demonstrate their further synthetic utility. With the ever expanding importance of glycoconjugates in various drug discovery programs, the molecular scaffolds that are presented in this work expand the repertoire of arsenal at the disposal of chemists working in this exciting area.

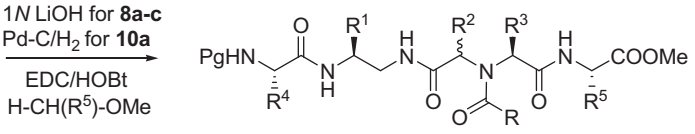
Acknowledgment

We thank the Board of Research in Nuclear Sciences (BRNS), Mumbai (No. 2011/37C/35/BRNS) for the financial assistance.



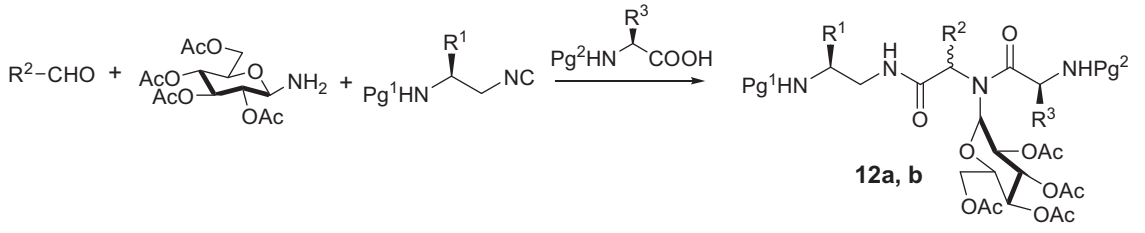
R = sugar acid **(5a-c)**
R = triazole acid **(7a)**

8a: Pg = Z; X = CH_3; R^1 = CH_3; R^2 = C_6H_5; R^3 = $CH_2C_6H_5$; R^4 = $CH_2C_6H_5$ (82%)
8b: Pg = Boc; X = CH_3; R^1 = $CH_2CH(CH_3)_2$; R^2 = $CH_2CH(CH_3)_2$; R^3 = $CH_2C_6H_5$; R^4 = CH_3 (83%)
8c: Pg = Z; X = CH_3; R^1 = $CH(CH_3)_2$; R^2 = C_4H_4O; R^3 = $(CH_2)_4NHBoc$; R^4 = H (85%)
10a: Pg = Fmoc; X = $CH_2C_6H_5$; R^1 = $(CH_2)_2SCH_3$; R^2 = C_4H_4O; R^3 = C_6H_5; R_4 = $CH(CH_3)_2$ (83%)



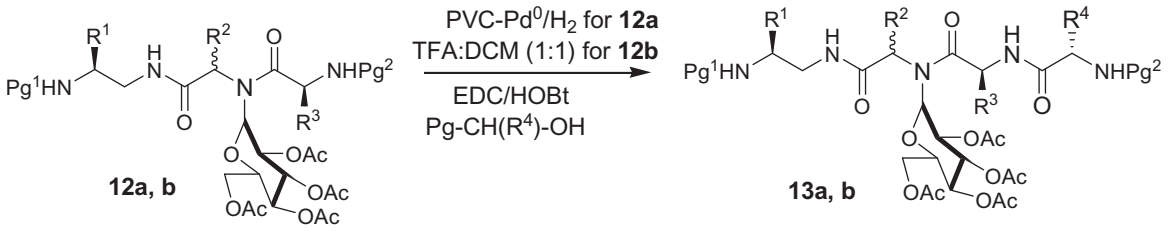
9a: Pg = Z; R^1 = CH_3; R^2 = C_6H_5; R^3 = $CH_2C_6H_5$; R^4 = $CH_2C_6H_5$; R_5 = CH_3 (85%)
9b: Pg = Boc; R^1 = $CH_2CH(CH_3)_2$; R^2 = $CH_2CH(CH_3)_2$; R^3 = $CH_2C_6H_5$; R^4 = CH_3; R_5 = H (81%)
9c: Pg = Z; R^1 = $CH(CH_3)_2$; R^2 = C_4H_4O; R^3 = $(CH_2)_4NHBoc$; R^4 = H; R^5 = C_6H_5 (82%)
11a: Pg = Fmoc; R^1 = $(CH_2)_2SCH_3$; R^2 = C_4H_4O; R^3 = C_6H_5; R^4 = $CH(CH_3)_2$; R^5 = CH_3 (79%)

Scheme 2. Chain extension on N-glycosylated peptidomimetics **5** and **7**.



	Pg^1	Pg^2	R^1	R^2	R^3	Yield (%)
12a	Fmoc	Z	$CH_2C_6H_5$	Ph	CH_3	88
12b	Z	Boc	CH_3	^{i}Bu	$CH(CH_3)_2$	85

Scheme 3. Synthesis of orthogonally protected N-glycosylated peptidomimetics.



	Pg^1	Pg^2	R^1	R^2	R^3	R^4	Yield (%)
13a	Fmoc	Boc	$CH_2C_6H_5$	Ph	CH_3	$CH(CH_3)_2$	85
13b	Z	Fmoc	CH_3	^{i}Bu	$CH(CH_3)_2$	$CH_2C_6H_5$	80

Scheme 4. Chain extension on orthogonally protected Ugi products **12a** and **12b**.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.06.013.

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24. *General procedure for the synthesis of compounds* ***5a–7c****:* The amine (1 mmol) and aldehyde (1 mmol), dissolved in 2 mL MeOH were stirred at rt until complete formation of imine (TLC analysis, 30 min). Then the isocyanide (1 mmol) and acid component (1 mmol) dissolved in MeOH (1 mL) were added to the reaction mixture and stirred for 2 days. After completion of the reaction as monitored by TLC the solvent was evaporated and compound was extracted into EtOAc (15 mL) washed with Na2CO3 (5%, 5 mL), citric acid (10%, 5 mL), water (5 mL), and brine, and dried over anhydrous Na_2SO_4. Evaporation of solvent in vacuo followed by column chromatography (EtOAc/hexane; 4:6) affords Ugi products **5a–7c**.
25. Chiral-HPLC analysis was carried out (Agilent 1100 series having G1311A VWD at $\lambda = 254$ nm, flow 1.0 mL/min, column: phenominex made Lux, pore size-5 μ, Cellusole-1, diameter × length = 250 × 4.6 mm; method: 85:15 *n*-hexane/isopropanol in isocratic mode, 40 min run). Chiral-HPLC profile of **5a** showed two peaks one at $R_t = 21.65$ min and another peak at $R_t = 27.23$ min in the ratio 97.5:2.5, respectively. Similarly, chiral-HPLC profile of **6a** had two peaks at $R_t = 18.63$ min and $R_t = 24.21$ min in the ratio 97:3. Also, chiral-HPLC analysis carried out on **7a** showed two peaks in the ratio 95:5 at $R_t = 14.56$ min and $R_t = 19.64$ min. **7b** had two peaks in the ratio 94:6 at $R_t = 16.54$ min and $R_t = 20.55$ min and **7c** showed two peaks at $R_t = 17.21$ min and $R_t = 22.35$ min in the ratio 95:5.
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27. Spectroscopic data for few representative compounds
Compound ***5a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.21–1.35 (m, 12H), 1.44 (d, $J = 6.2$ Hz, 3H), 3.33–3.43 (m, 4H), 3.62 (s, 3H), 4.01–4.36 (m, 6H), 4.64–4.76 (m, 3H), 5.33 (m, 1H), 5.68 (s, 1H), 7.25–7.45 (m, 18H), 7.69–7.76 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 18.6, 26.1, 35.9, 45.2, 47.3, 47.7, 51.4, 52.6, 60.8, 60.9, 67.5, 70.3, 70.5, 70.9, 96.8, 109.1, 110.1, 126.1, 126.4, 127.0, 127.6, 127.7, 127.9, 128.3, 128.8, 129.1, 129.3, 129.9, 130.7, 141.2, 143.9, 155.9, 168.2, 170.3, 170.9; HR-MS calcd for $C_{48}H_{53}N_3O_{11}$ *m*/*z* 870.3578 [M+Na]$^+$, found 870.3571.
Compound ***6a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.98 (d, $J = 6.4$ Hz, 6H), 1.71 (m, 2H), 1.81 (m, 2H), 3.12 (d, $J = 6.2$ Hz, 2H), 3.45 (m, 3H), 3.65 (s, 3H), 4.11 (s, 2H), 4.43 (t, $J = 4.8$ Hz, 1H), 4.50 (m, 2H), 4.61 (d, $J = 6.4$ Hz, 2H), 4.75 (m, 1H), 4.81 (m, 1H), 5.15 (m, 1H), 5.25 (s, 2H), 5.34 (m, 1H), 6.11 (br s, 1H), 6.99 (m, 2H), 7.25–7.50 (m, 30H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 20.2, 21.5, 37.8, 41.3, 44.1, 44.3, 44.8, 50.1, 51.8, 52.5, 64.8, 65.1, 70.5, 71.2, 72.2, 73.1, 76.5, 125.9, 127.1, 127.8, 128.2, 128.6, 128.9, 129.3, 129.8, 130.5, 137.8, 140.9, 155.8, 165.1, 166.5, 168.9, 171.2; HR-MS calcd for $C_{62}H_{64}N_4O_{15}$ *m*/*z* 1127.4266 [M+Na]$^+$, found 1127.4269.
Compound ***7a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.27 (s, 9H), 1.81 (m, 2H), 1.99 (s, 12H), 2.11 (s, 3H), 2.38 (t, $J = 4.8$ Hz, 2H), 3.35 (m, 2H), 4.12 (m, 1H), 4.25 (d, $J = 5.2$ Hz, 2H), 4.51 (m, 1H), 4.68 (m, 1H), 4.71 (m, 1H), 5.12 (m, 1H), 5.25 (s, 2H), 5.68 (s, 1H), 6.01 (m, 1H), 6.12 (s, 1H), 6.20 (m, 1H), 6.25 (d, $J = 5.8$ Hz, 1H), 7.05–7.25 (m, 11H), 6.98 (br s, 2H), 8.11 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 16.8, 20.5, 27.9, 28.3, 30.5, 43.1, 49.8, 52.5, 55.3, 58.1, 65.1, 67.7, 70.8, 71.3, 75.2, 78.9, 89.3, 105.6, 109.8, 126.7, 128.9, 129.8, 131.5, 134.5, 141.8, 143.7, 152.3, 155.5, 162.1, 168.5, 170.1, 171.5; ESI-MS calcd for $C_{48}H_{58}N_6O_{16}S$ *m*/*z* 1029.35 [M+Na]$^+$, found 1029.40.
Compound ***8a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.18 (s, 3H), 1.45 (s, 12H), 3.01 (d, $J = 5.2$ Hz, 2H), 3.25 (d, $J = 5.2$ Hz, 2H), 3.51 (m, 2H), 3.65 (s, 3H), 4.12 (m, 1H), 4.21 (m, 1H), 4.35 (m, 1H), 4.48 (d, $J = 5.6$ Hz, 1H), 4.85–4.93 (m, 3H), 5.12 (d, $J = 5.2$ Hz, 1H), 5.35 (s, 2H), 5.51 (s, 1H), 6.91–6.99 (m, 3H), 7.12–7.20 (m, 20H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 19.1, 25.1, 33.8, 36.9, 45.3, 51.2, 52.5, 54.4, 58.6, 63.3, 65.1, 66.2, 67.2, 71.1, 71.9, 98.9, 106.9, 109.8, 125.7, 127.1, 127.7, 128.6, 129.1, 129.7, 135.7, 139.4, 141.1, 155.5, 168.1, 169. 3, 171.5; HR-MS calcd for $C_{50}H_{58}N_4O_{12}$ *m*/*z* 929.3949 [M+Na]$^+$, found 929.3944.
Compound ***9b****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.95 (d, $J = 6.0$ Hz, 12H), 1.37 (s, 9H), 1.43 (s, 12H), 1.45–1.51 (m, 5H), 1.62 (m, 2H), 1.81 (m, 2H), 2.99 (d, $J = 5.4$ Hz, 2H), 3.25 (m, 2H), 3.65 (s, 3H), 4.11 (d, $J = 4.8$ Hz, 2H), 4.25 (m, 2H), 4.40 (m, 1H), 4.55 (m, 2H), 4.81–4.88 (m, 3H), 5.15 (d, $J = 5.0$ Hz, 1H), 6.85–6.91 (m, 4H), 7.05–7.21 (m, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 18.1, 21.2, 21.5, 22.7, 22.8, 26.4, 28.1, 34.8, 37.9, 39.5, 41.3, 44.8, 45.9, 49.3, 50.4, 51.0, 52.3, 66.2, 66.8, 71.5, 72.1, 78.9, 98.7, 125.7, 127.1, 128.5, 155.5, 168.5, 169.6, 171.5, 172.0; HR-MS calcd for $C_{44}H_{69}N_5O_{13}$ *m*/*z* 898.4790 [M+Na]$^+$, found 898.4795.
Compound ***11a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.99 (d, $J = 5.6$ Hz, 6H), 1.29 (d, $J = 5.2$ Hz, 3H), 1.81 (m, 2H), 2.05 (s, 15H), 2.31 (t, $J = 4.8$ Hz, 2H), 2.61 (m, 1H), 3.12 (m, 2H), 3.66 (s, 3H), 4.12 (d, $J = 4.6$ Hz, 2H), 4.25 (m, 1H), 4.35 (t, $J = 4.2$ Hz, 1H), 4.50 (m, 1H), 4.58 (d, $J = 5.0$ Hz, 1H), 4.63 (m, 1H), 4.68 (m, 1H), 4.73 (m, 1H), 4.80 (d, $J = 5.0$ Hz, 2H), 5.13 (m, 1H), 5.35 (s, 1H), 5.98 (s, 1H), 6.04 (d, $J = 5.4$ Hz, 1H), 6.12 (m, 1H), 6.29 (d, $J = 5.6$ Hz, 1H), 6.98–7.04 (m, 4H), 7.17–7.68 (m, 14H), 8.12 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 17.5, 17.7, 18.0, 20.9, 30.1, 30.8, 31.5, 42.5, 46.6, 47.1, 48.5, 52.5, 54.8, 57.5, 59.5, 65.6, 67.4, 68.1, 71.0, 72.1, 75.2, 91.3, 105.3, 110.4, 125.1, 126.7, 127.1, 128.0, 128.5, 129.0, 129.5, 131.0, 135.6, 141.1, 141.9, 143.5, 143.9, 151.6, 155.6, 161.8, 168.5, 168.9, 170.1, 170.9, 171.5; HR-MS calcd for $C_{60}H_{70}N_8O_{18}S$ *m*/*z* 1245.4426 [M+Na]$^+$, found 1245. 4430.
Compound ***12a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.21 (d, $J = 6.8$ Hz, 3H), 1.99 (s, 12H), 2.56 (d, $J = 6.2$ Hz, 2H), 3.35 (m, 2H), 4.12 (t, $J = 4.8$ Hz, 1H), 4.25 (m, 2H), 4.45 (d, $J = 5.8$ Hz, 2H), 4.61 (m, 1H), 4.75 (m, 1H), 4.77 (m, 1H), 4.81 (m, 1H), 5.08 (m, 1H), 5.24 (s, 2H), 5.29 (m, 1H), 5.45 (m, 1H), 6.11 (m, 1H), 7.18–7.72 (m, 23H), 7.79–7.82 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 19.1, 21.3, 21.5, 39.8, 43.5, 47.5, 49.5, 51.5, 52.8, 62.9, 65.1, 67.6, 68.0, 68.5, 68.9, 71.9, 79.5, 125.0, 125.5, 126.0, 126.2, 126.4, 126.5, 126.9, 127.1, 127.3, 127.5, 127.7, 127.9, 128.1, 128.4, 128.7, 128.8, 129.0, 135.1, 138.5, 139.8, 141.5, 143.6, 155.8, 156.5, 168.5, 170.5, 171.0; HR-MS calcd for $C_{57}H_{60}N_4O_{15}$ *m*/*z* 1063.3953 [M+Na]$^+$, found 1063. 3960.
Compound ***13a****:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.00 (d, $J = 6.2$ Hz, 6H), 1.21 (d, $J = 5.8$ Hz, 3H), 1.32 (s, 9H), 2.01 (s, 12H), 2.59 (m, 1H), 2.71 (d, $J = 6.4$ Hz, 2H), 3.32 (m, 2H), 4.21 (d, $J = 6.2$ Hz, 2H), 4.35 (t, $J = 4.8$ Hz, 1H), 4.51 (m, 1H), 4.59 (m, 1H), 4.64 (m, 1H), 4.69 (d, $J = 6.0$ Hz, 2H), 4.73 (m, 2H), 5.21–5.28 (m, 2H), 5.31 (m, 1H), 6.12 (d, $J = 6.6$ Hz, 1H), 6.91–6.99 (br s, 4H), 7.25–7.77 (m, 18H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 17.0, 18.1, 20.9, 27.5, 30.0, 41.2, 43.4, 47.1, 51.3, 53.8, 57.7, 64.5, 67.1, 68.5, 69.8, 71.3, 72.5, 78.4, 125.1, 126.7, 127.1, 128.2, 128.4, 128.8, 129.3, 129.7, 135.1, 137.8, 141.3, 143.5, 155.6, 156.1, 168.5, 170.1, 171.3; HR-MS calcd for $C_{59}H_{71}N_5O_{16}$ *m*/*z* 1128.4794 [M+Na]$^+$, found 1128.4798.